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DATE: Monday, April 10, 2006

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☐	L5	L4 same l2	19
☐	L4	(HMGB$ or HMG$) adj (anti or antibod$ or mab)	45
☐	L3	l2 same inflammation	161
☐	L2	(HMGB$ or HMG$) same cytokine	430
☐	L1	Newman-walter.in.	61

END OF SEARCH HISTORY

L4 ANSWER 418 OF 549 LIFESCI COPYRIGHT 2006 CSA on STN DUPLICATE 82
ACCESSION NUMBER: 1999:74851 LIFESCI
TITLE: HMG-1 as a late mediator of endotoxin lethality in mice
AUTHOR: Wang, H.; Bloom, O.; Zhang, Minghuang; Vishnubhakat, J.M.; Ombrellino, M.; Che, Jiantu; Frazier, A.; Yang, H.; Ivanova, S.; Borovikova, L.; Manogue, K.R.; Faist, E.; Abraham, E.; Tracey, K.J.; et al.
CORPORATE SOURCE: Dep. Emerg. Med., North Shore Univ. Hosp.-New York Univ. Sch. Med., Manhasset, NY 11030, USA; E-mail: hwang@picower.edu
SOURCE: Science (Washington) [Science (Wash.)], (19990709) vol. 285, no. 5425, pp. 248-251.
ISSN: 0036-8075.
DOCUMENT TYPE: Journal
FILE SEGMENT: F; J; X; N
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Endotoxin, a constituent of Gram-negative bacteria, stimulates macrophages to release large quantities of tumor necrosis factor (**TNF**) and interleukin-1 (IL-1), which can precipitate tissue injury and lethal shock (endotoxemia). Antagonists of **TNF** and IL-1 have shown limited efficacy in clinical trials, possibly because these **cytokines** are early mediators in pathogenesis. Here a potential late mediator of lethality is identified and characterized in a mouse model. High mobility group-1 (**HMG**-1) protein was found to be released by cultured macrophages more than 8 hours after stimulation with endotoxin, **TNF**, or IL-1. Mice showed increased serum levels of **HMG** -1 from 8 to 32 hours after endotoxin exposure. Delayed administration of **antibodies** to **HMG**-1 attenuated endotoxin lethality in mice, and administration of **HMG**-1 itself was lethal. Septic patients who succumbed to infection had increased serum **HMG**-1 levels, suggesting that this protein warrants investigation as a therapeutic target.
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L4 ANSWER 417 OF 549 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1999:29382808 BIOTECHNO

TITLE: Proinflammatory cytokines (tumor necrosis factor and interleukin 1) stimulate release of high mobility group protein-1 by pituicytes

AUTHOR: Wang H.; Vishnubhakat J.M.; Bloom O.; Zhang M.; Ombrellino M.; Sama A.; Tracey K.J.

CORPORATE SOURCE: Dr. H. Wang, North Shore University Hospital, New York Univ. School of Medicine, Picower Inst. for Medical Research, 350 Community Dr, Manhasset, NY 11030, United States.

SOURCE: Surgery, (1999), 126/2 (389-392), 13 reference(s)
CODEN: SURGAZ ISSN: 0039-6060

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background. **Cytokines** mediate the metabolic and physiologic responses to injury and infection. Anterior pituitary cells express receptors for tumor necrosis factor (**TNF**) and interleukin 1 (IL-1), which can signal these cells to release corticotropin, growth hormone, and **cytokines** such as IL-1 and macrophage migration inhibitory factor. This interaction provides an important link between the immune system and the neuroendocrine system. We reasoned that pituicytes activated with **TNF** or IL-1 might release previously unrecognized factors that could participate in this signaling from the neuroendocrine to the immune system. Methods. Proteins released from rat pituicytes (GH.sub.3) after stimulation with proinflammatory **cytokines** were identified by N-terminal amino acid sequencing. Polyclonal **antibodies** against a peptide corresponding to the N-terminal amino acid sequence were generated and used to determine the kinetics of protein release. Results. **Cytokine** stimulation induced the release of a 30-kd protein from rat pituicytes. After the protein was isolated and the N-terminal amino acid sequence determined, a protein database analysis revealed that it is high mobility group-1 (**HMG**-1) protein. **TNF** and IL-1 induced the release of **HMG**-1 from pituicytes in a time- and dose-dependent manner. Interferon gamma alone did not induce the release of **HMG**-1, but it enhanced **TNF**-induced **HMG**-1 release. Conclusion. Stimulation of pituicytes by **TNF** or IL-1 induces the release of **HMG**-1, which may participate in the regulation of neuroendocrine and immune responses to infection or injury.

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L4 ANSWER 410 OF 549 PHIN COPYRIGHT 2006 T&F Informa UK Ltd on STN

ACCESSION NUMBER: 1999:13443 PHIN
DOCUMENT NUMBER: S00630876
DATA ENTRY DATE: 23 Jul 1999
TITLE: Possible new target for septic shock
SOURCE: Scrip (1999) No. 2457 p22
DOCUMENT TYPE: Newsletter
FILE SEGMENT: FULL
TX The scientists, from the US, Germany and Sweden, say that these clinical trials may have failed because **cytokines** such as **TNF** are early mediators in the pathogenesis of shock. They have now characterised a late mediator of shock, known as high mobility group-1 protein (**HMG**-1), which they found to be released by macrophages in culture eight hours after stimulation with endotoxin. In mice models of shock, the administration of **antibodies** to **HMG**-1 attenuated endotoxin death, while the protein itself was lethal (Science, July 9th, p 248).

L4 ANSWER 407 OF 549 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2000:30728141 BIOTECHNO

TITLE: Cutting edge: HMG-1 as a mediator of acute lung inflammation

AUTHOR: Abraham E.; Arcaroli J.; Carmody A.; Wang H.; Tracey K.J.

CORPORATE SOURCE: Dr. E. Abraham, Div. Pulmon. Sci./Critical Care Med., Univ. of Colorado Hlth. Sci. Center, Box C272, 4200 East Ninth Avenue, Denver, CO 80262, United States. E-mail: edward.abraham@uchsc.edu

SOURCE: Journal of Immunology, (15 SEP 2000), 165/6 (2950-2954), 25 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Acute inflammatory lung injury is often a delayed complication of critical illness and is associated with increased mortality. High mobility group-1 (**HMG**-1) protein, in addition to its role as a transcriptional regulatory factor, has recently been identified as a late mediator of endotoxin lethality. In the present studies, **HMG**-1 given intratracheally produced acute inflammatory injury to the lungs, with neutrophil accumulation, the development of lung edema, and increased pulmonary production of IL-1β, **TNF**-α, and macrophage-inflammatory protein-2. In endotoxin-induced acute lung inflammation, administration of **anti-HMG**-1 Abs either before or after endotoxin exposure decreased the migration of neutrophils to the lungs as well as lung edema. These protective effects of **anti-HMG**-1 were specific, because pulmonary levels of IL-1β, **TNF**-α, or macrophage-inflammatory protein-2 were not decreased after therapy with **anti-HMG**-1. Together, these findings indicate that **HMG**-1 is a distal mediator of acute inflammatory lung injury.

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L4 ANSWER 397 OF 549 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2001254670 ESBIOBASE
TITLE: Dual roles for HMGB1: DNA binding and cytokine
AUTHOR: Czura C.J.; Wang H.; Tracey K.J.
CORPORATE SOURCE: Dr. K.J. Tracey, Center for Patient-Oriented Research, Laboratory of Biomedical Science, North Shore/LIJ Research Institute, 350 Community Drive, Manhasset, NY 11030, United States.
E-mail: kjtracey@sprynet.com
SOURCE: Journal of Endotoxin Research, (2001), 7/4 (315-321), 79 reference(s)
CODEN: JENREB ISSN: 0968-0519
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Effective therapies against overwhelming Gram-negative bacteremia, or sepsis, have eluded successful development. The discovery that tumor necrosis factor (**TNF**), a host-derived inflammatory mediator, was both necessary and sufficient to recapitulate Gram-negative sepsis raised cautious optimism for developing a targeted therapeutic. However, the rapid kinetics of the **TNF** response to infection defined an extremely narrow window of opportunity during which **anti-TNF** therapeutics could be successfully administered. **HMGB1** was previously studied as a DNA-binding protein involved in DNA replication, repair, and transcription; and as a membrane-associated protein that mediates neurite outgrowth. A decade-long search has culminated in our identification of **HMGB1** as a late mediator of endotoxemia. **HMGB1** is released by macrophages upon exposure to endotoxin, activates many other pro-inflammatory mediators, and is lethal to otherwise healthy animals. Elevated levels of **HMGB1** are observed in the serum of patients with sepsis, and the highest levels were found in those patients that died. The delayed kinetics of **HMGB1** release indicate that it may be useful to target this toxic **cytokine** in the development of future therapies.

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CORPORATE SOURCE: Dr. K.J. Tracey, Center for Patient-Oriented Research, Laboratory of Biomedical Science, North Shore/LIJ Research Institute, 350 Community Drive, Manhasset, NY 11030, United States.
E-mail: kjtracey@sprynet.com
SOURCE: Journal of Endotoxin Research, (2001), 7/4 (315-321), 79 reference(s)
CODEN: JENREB ISSN: 0968-0519
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

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